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EARLY DIFFERENTIAL DIAGNOSIS BETWEEN HYPERTROPHIC AND NONHYPERTROPHIC HEALING*

HUGO A. LINARES, M.D., AND DUANE L. LARSON, M.D.†

ABSTRACT

The development of scars in 121 burned children, 1–16 years old, was studied by examining 252 biopsies of granulation tissue. The range in age of the granulation tissue subsequent to the initial injury was from 20 to more than 120 days. The follow-up data of the patients spanned a period from 2 months to 4 years after burn.

One hundred of the patients developed hypertrophic scars and their granulation tissue showed collagen fibers in a whorl-like or nodular arrangement. This was in contrast to the parallel orientation of collagen fibers seen in the granulation tissue of the 21 patients who developed nonhypertrophic scars. The orientation of the collagen fibers in the granulation tissue may thus serve as a prognostic index to the type of scar that will develop.

Previous work has demonstrated that the factors responsible for deviation in the normal wound healing process are found within the granulation tissue and that events differentiating hypertrophic scars from nonhypertrophic scars actually start from the moment of injury [1]. Although hypertrophic scars have been studied in animals [2] and have been reproduced in certain experimental conditions [3], a laboratory model capable of consistently developing hypertrophic scars is not available. Due to this limitation we started a few years ago the study of granulation tissue and subsequent scar development in burned children in whom the appearance of hypertrophic scarring is so frequent. During four years we have studied biopsies of granulation tissue by light microscopy and have been able to follow its evolution serially in individual patients until the development of normal scar or hypertrophic scar became evident.

This paper will discuss those observations that are primarily related to the arrangement of the collagen fibers. Because, like other workers [4, 5] we support the opinion that hypertrophic scars and keloids are lesions of different magnitudes which result from the same morbid process, no distinction will be made between these types of scars.

MATERIALS AND METHODS

Biopsies were obtained from post-burn granulation tissue in 121 children treated at our Institution. The ages of the children ranged from 1–16 years. Biopsies were taken from several anatomic areas and in some cases two or more biopsies were available from the same patient, taken at different times during the evolution of the wound. The age of the granulation tissue taken from the area of injury ranged from 20 days to more than 120 days. The availability of chronic granulation tissue from areas receiving primary grafts as well as tissue from areas being regrafted following the partial or total loss of the primary graft made it possible to follow changes over a relatively long evolutionary period.

All of the specimens were fixed in 10% buffered formalin. The following stains were used: (1) hematoxylin–eosin, (2) Masson and Gallego's stain for general morphology, (3) Gridley's method for collagen and reticular fibers.

TABLE

Classification of patients and biopsies by sex and race

	Scar development	White		Black		Brown*		Total
		M	F	M	F	M	F	
Patients	Hypertrophic	54	29	8	3	3	3	100
	Nonhypertrophic	13	1	1	3	1	2	21
Biopsies	Hypertrophic	119	67	15	3	3	7	214
	Nonhypertrophic	24	2	2	3	2	5	38

* The brown color refers to Latin Americans descended from Latin-American Indians.

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* From the Division of Pathology and †Division of Surgery, Shriners Burns Institute, Galveston, Texas 77550.

RESULTS

Patients Who Did Not Develop Hypertrophic Scars

Twenty-one of the patients examined did not develop hypertrophic scars (Table). Study of the 38 biopsies available from these patients showed a similar pattern to that observed in normal wound healing. The newly formed vessels of the young granulation tissue had a predominantly vertical orientation with respect to the open surface. The

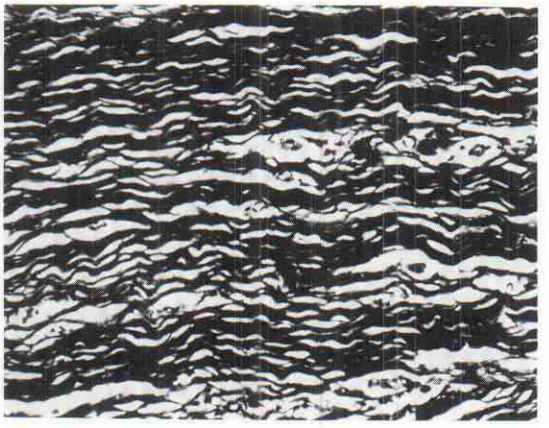

FIG. 1: Area of nonhypertrophic scar. Note the predominant parallel orientation of the collagen fibers of the reticular layer. Masson's stain, orig. mag. × 156.25.

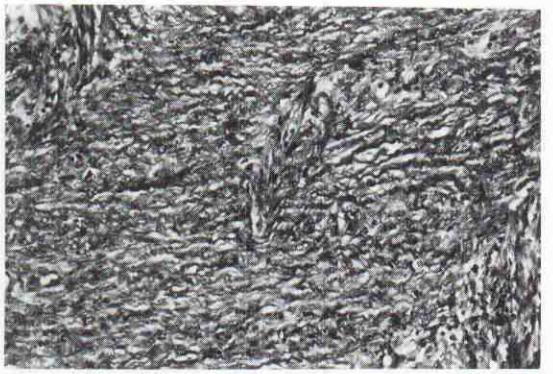

FIG. 2: Histologic section of granulation tissue from patient in Figure 3. Note the predominant parallel orientation of the collagen fibers. Masson's stain, orig. mag. × 156.25.

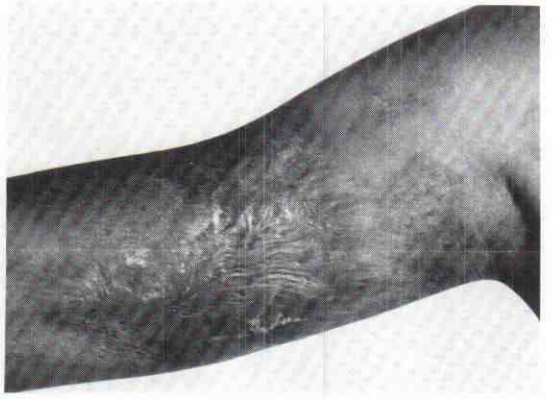

FIG. 3: Patient from whom tissue in Figure 2 was obtained. Note nonhypertrophic healing, wrinkles, and soft tissue. 142 days post burn.

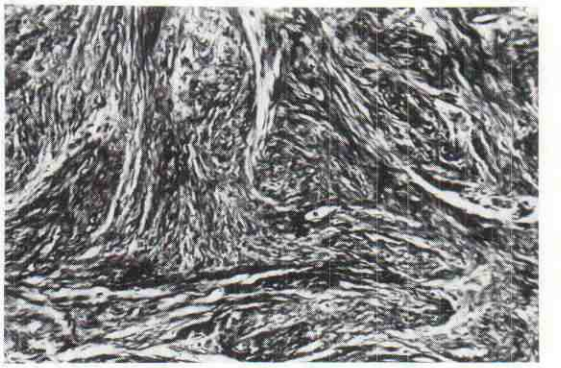

FIG. 4: Area of hypertrophic scar. Collagen fibers are oriented in a predominant whorl-like or nodular pattern. Masson's stain, orig. mag. × 156.25.

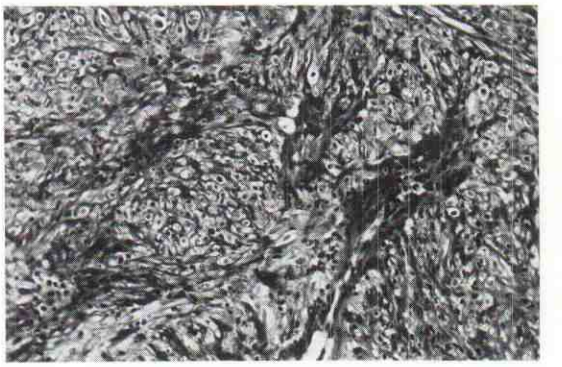

FIG. 5: Histologic section of granulation tissue from patient in Figure 6. Note the histologic appearance of a whorl-like pattern. Masson's stain, orig. mag. × 156.25.

FIG. 6: Patient from whom tissue in Figure 5 was obtained. Note hypertrophic healing. 125 days post burn.

young connective tissue, primarily fibroblasts and collagen fibers, also followed a typical pattern. At the surface these structures were parallel to the vertical proliferating capillaries. In the lower layers, however, they had a transverse orientation with respect to the vessels, lying parallel to the base of the wound. This pattern of collagen fibers is consistent with the histologic appearance of normal granulation tissue and is similar to the arrangement of the collagen fibers in the reticular layer of the dermis of the nonhypertrophic scars which developed in these patients. In these scars the collagen fibers have predominantly a parallel orientation to the surface (Fig. 1) in contrast with normal dermis where the collagen fibers of the reticular layer are arranged in a tridimensional meshwork.

Figures 2 and 3 show one of the cases studied. Figure 2 illustrates the orientation of the collagen fibers in a predominantly parallel orientation as seen in the microscopic examination of the granulation tissue, 20 days after burn. Figure 3 shows the same patient 122 days later when the development of the nonhypertrophic scar is obvious.

Patients Who Develop Hypertrophic Scars

Of the 121 patients studied, 100 developed hypertrophic scars. The histologic morphology of the granulation tissue from these patients was quite different from that of the previous group. The most notable difference was the orientation of the collagen fibers. Even in the earliest stages it was possible to see a tendency for the collagen fibers to assume a whorl-like or nodular pattern. This morphologic characteristic, consistently present in the dermis of hypertrophic scars (Fig. 4), has been described previously [6].

Figures 5 and 6 show one of the cases. Figure 5 shows the histologic appearance of the whorl-like arrangement in the granulation tissue, 23 days after burn. Figure 6 illustrates the appearance of the hypertrophic scar 102 days later.

DISCUSSION

A predominant parallel arrangement of the collagen fibers of the reticular layer of the dermis is characteristic of the nonhypertrophic scars and the most consistent histologic pattern for hypertrophic scars is the arrangement of the collagen matrix in the form of whorls or nodules [4, 6]. This peculiar orientation of the collagen fibers was also observed in biopsies of granulation tissue [1].

All of the patients of this study who showed granulation tissue with collagen fibers in whorls or nodules developed hypertrophic scars. On the other hand, those patients who did not show whorls or nodules did not develop hypertrophic scars. Thus, the results of this period of four years of investigation on granulation tissue and scars lead us to conclude: (1) The predisposing factors for production of hypertrophic scars act from the early stages of the wound healing. (2) An intensive investigation of the granulation tissue may be an invaluable approach to clarify the hypertrophic scar problem. (3) Control during the early phase of wound healing could possibly prevent or at least diminish the development of hypertrophic scars [7].

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